stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 10 micrograms of cephradine per milliliter (estimated).

(ii) *Hydroxylamine colorimetric assay*. Proceed as directed in §442.40(b)(1)(ii). If packaged for dispensing, reconstitute the sample as directed in the labeling using distilled water instead of the reconstituting fluid. Further dilute an aliquot of this solution with distilled water to 1 milligram of cephradine per milliliter (estimated).

(iii) *High-pressure liquid chromatographic assay*. Proceed as directed in §436.337 of this chapter.

(2) *Sterility*. Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in §436.32(g) of this chapter, using a solution containing 80 milligrams of cephradine per milliliter.

(4) [Reserved]

(5) *Moisture.* Proceed as directed in §436.201 of this chapter.

(6) *pH*. Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(7) *Cephalexin content.* Proceed as directed in §442.40(b)(5).

(8) *Identity*. Proceed as directed in §436.211 of this chapter, using the 1 percent potassium bromide disc prepared as described in paragraph (b)(1) of that section.

(9) *Crystallinity*. Proceed as directed in §436.203(a) of this chapter.

[40 FR 51626, Nov. 6, 1975, as amended at 43 FR 14646, Apr. 7, 1978; 49 FR 47485, Dec. 5, 1984; 50 FR 19919, May 13, 1985]

§442.41 Cephradine dihydrate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Cephradine dihydrate is the dihydrate form of (6*R*,7*R*)-7-[(*R*)-2-amino-2-(1,4-cyclohexadien-1-yl)acetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms and not more than 1,050 micrograms of cephradine per milligram on an anhydrous basis.

(ii) [Reserved]

(iii) Its moisture content is not less than 8.5 percent and not more than 10.5 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 3.5 and not more than 6.0.

(v) Its cephalexin content is not more than 5 percent on an anhydrous basis.

(vi) It passes the identity test.

(vii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, cephalexin content, identity, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 500 milligrams.

(b) *Tests and methods of assay*—(1) *Potency*. Use any of the following methods; however, the results obtained from the hydroxylamine colorimetric assay shall be conclusive.

(i) *Microbiological agar diffusion assay*. Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 10.0 micrograms of cephradine per milliliter (estimated).

(ii) *Hydroxylamine colorimetric assay for cephradine.* Proceed as directed in §442.40(b)(1)(ii).

(iii) *High-pressure liquid chromatographic assay*. Proceed as directed in §436.337 of this chapter, preparing the sample as described in paragraph (e)(3)(i) of that section.

(2) [Reserved]

(3) *Moisture.* Proceed as directed in §436.201 of thichapter.

(4) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(5) *Cephalexin content.* Proceed as directed in § 436.337 of this chapter.

(6) *Identity.* Proceed as directed in § 436.211 of this chapter, using the 1 percent potassium bromide disc prepared as described in paragraph (b)(1) of that section.

(7) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[47 FR 11856, Mar. 19, 1982, as amended at 49 FR 47485, Dec. 5, 1984; 50 FR 19919, May 13, 1985]

§ 442.50a Sterile ceforanide.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Ceforanide is 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[[2-(amino-methyl)phenyl]acetyl]amino]-3-[[[1-(carboxymethyl)-1*H*-tetrazol-5-yl]-thio]methyl]-8-oxo-,(6*R-trans*)-. It is a white to off-white powder. It is so purified and dried that:

(i) Its ceforanide content is not less than 900 micrograms and not more than 1,050 micrograms of ceforanide per milligram.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) Its moisture content is not more than 5.0 percent.

(v) Its pH in an aqueous suspension containing 50 milligrams per milliliter is not less than 2.5 and not more than 4.5.

(vi) It passes the identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for ceforanide content, sterility, pyrogens, moisture, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(*a*) For all tests except sterility: 10 packages, each containing approximately 500 milligrams.

(*b*) For sterility testing: One package containing approximately 6 grams of a composite sample.

(b) *Tests and methods of assay*—(1) *Ceforanide content.* Proceed as directed in § 436.348 of this chapter, preparing the sample and calculating the ceforanide content as follows:

(i) *Preparation of sample solution.* Prepare a solution containing 1.0 milligram per milliliter in mobile phase. Inject each sample within 5 minutes after dissolution.

(ii) *Calculations.* Calculate the micrograms of ceforanide per milligram of sample as follows:

$$\text{Micrograms of ceforanide per milligram} = \frac{A_u \times P_s}{A_s \times C_u}$$

where:

A_u = Area of the ceforanide peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s = Area of the ceforanide peak in the chromatogram of the ceforanide working standard;

P_s = Ceforanide activity in the ceforanide working standard solution in micrograms per milliliter; and

C_u = Milligrams of sample per milliliter of sample solution.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except:

(i) In paragraph (e)(1)(i)(*a*) of that section, use diluting fluid G in lieu of diluting fluid A; and

(ii) In lieu of three 100-milliliter quantities of diluting fluid A in paragraph (e)(2) of that section, filter three 100-milliliter quantities of diluting fluid D followed by a 100-milliliter quantity of diluting fluid A.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, except suspend 1 gram of sterile ceforanide in 12.5 milliliters of pyrogen-free water (diluent 1). Add 320 milligrams of pyrogen-free *L*-lysine base, shake to dissolve the mixture. If the mixture is not dissolved, add an amount of *L*-lysine necessary to obtain a solution. The test sample should contain not more than a total of 340 milligrams of *L*-lysine. Dilute the resulting solution to 20 milliliters. Use a test dose of 1 milliliter of the 50 milligrams per milliliter test solution per kilogram of rabbit weight.

(4) *Moisture.* Proceed as directed in § 436.201 of this chapter.